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NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
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NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
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NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
now available on STN
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NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
NEWS 25 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 26 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27 Oct 21 EVENTLINE has been reloaded
NEWS 28 Oct 24 BEILSTEIN adds new search fields
NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 31 Nov 18 DKILIT has been renamed APOLLIT
NEWS 32 Nov 25 More calculated properties added to REGISTRY
NEWS 33 Dec 02 TIBKAT will be removed from STN
NEWS 34 Dec 04 CSA files on STN
NEWS 35 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36 Dec 17 TOXCENTER enhanced with additional content
NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN
NEWS 38 Dec 30 ISMEC no longer available
NEWS 39 Jan 13 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003
NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003
NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,

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ENERGY, INSPEC

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
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=> FIL REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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STRUCTURE FILE UPDATES: 28 JAN 2003 HIGHEST RN 482573-45-5

DICTIONARY FILE UPDATES: 28 JAN 2003 HIGHEST RN 482573-45-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s wevlcwtwetcer/sqsp

L1 7 WEVLCWTWETCER/SQSP

=> FIL BIOSIS MEDLINE CAPLUS EMBASE SCISEARCH PCTFULL USPATFULL USPAT2 EUROPATFULL

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

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=> s l1

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L2 3 L1

=> d 12 py pn au ti so ab

L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
PY 2001

AU Roberge, Martin; Santell, Lydia; Dennis, Mark S.; Eigenbrot, Charles;
Dwyer, Mary A.; Lazarus, Robert A.

TI A novel exosite on coagulation factor VIIa and its molecular interactions
with a new class of peptide inhibitors

SO Biochemistry (2001), 40(32), 9522-9531
CODEN: BICHAW; ISSN: 0006-2960

AB A new inhibitory peptide binding exosite on the protease domain of
coagulation Factor VIIa (FVIIa) has been identified. A novel series of
peptide inhibitors of FVIIa, termed the "A-series" peptides, identified
from peptide phage libraries and exemplified by peptide A-183,
specifically bind at a site that is distinct from both the active site and
the exosite of another recently described peptide inhibitor of FVIIa;
E-76. Peptide A-183 prolonged TF-dependent clotting in human, but not
rabbit plasma. Thus, a panel of human FVIIa mutants, contg. 70 of the 76
rabbit sequence differences in the protease domain, localized the binding
site to residues in the 60s loop and the C-terminus. The location of the
exosite was refined by a series of FVIIa alanine mutants, which showed
that proximal residues Trp 61 and Leu 251 were crit. for binding. Kinetic
and equil. binding consts. for zymogen FVII, FVIIa and TF.cntdot.FVIIa

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were detd. using immobilized N-terminal biotinylated A-183 by surface plasmon resonance. No peptide binding to nine other human serine proteases was obsd. Key residues on the peptide were detd. from binding to FVIIa and inhibition of FX activation using a series of alanine mutants of A-183 fused to the Z domain of protein A. Anal. of the mutagenesis data is presented in the context of a crystal structure of A-183 in complex with a version of zymogen FVII. The shape and proximity of this exosite to the active site may lend itself towards the design of new anticoagulants that inhibit FVIIa.

=> d l2 py pn au ti so ab 2-3

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

PY 2001

AU Dennis, Mark S.; Roberge, Martin; Quan, Cliff; Lazarus, Robert A.

TI Selection and characterization of a new class of peptide exosite inhibitors of coagulation factor VIIa

SO Biochemistry (2001), 40(32), 9513-9521

CODEN: BICHAW; ISSN: 0006-2960

AB A new series of peptide inhibitors of human Factor VIIa (FVIIa) has been identified and affinity matured from naive and partially randomized peptide phage libraries selected against the immobilized tissue factor.cntdot.Factor VIIa (TF.cntdot.FVIIa) complex. These "A-series" peptides contain a single disulfide bond and a 13-residue minimal core required for maximal affinity. They are exemplified by peptide A-183 (EEWEVLCWTWETCER), which binds at a newly identified exosite on the FVIIa protease domain, described in the accompanying report [Roberge, M., Santell, L., Dennis, M. S., Eigenbrot, C., Dwyer, M. A., and Lazarus, R. A. (2001) Biochem. 40, XXXXX-XXXXX]. A-183 was obtained from a trypsin digest of A-100-Z, a recombinant protein comprising A-183 and the Z domain of protein A. Surprisingly, A-183 was a very potent inhibitor of TF.cntdot.FVIIa, inhibiting activation of Factor X (FX) and Factor IX and amidolytic activity of Chromozym t-PA with IC50 values of 1.6 +/- 1.2, 3.5 +/- 0.3, and 8.5 +/- 3.5 nM, resp. Kinetic anal. revealed that A-183 was a partial (hyperbolic) mixed-type inhibitor of FX activation having a Ki of 200 pM as well as a partial competitive inhibitor of amidolytic activity. The A-series peptides were also specific and potent inhibitors of TF-dependent clotting as measured in a prothrombin time (PT) clotting assay and had no effect on the TF-independent activated partial thromboplastin time. At satg. concns. of peptide, the maximal extent by which A-183 and A-100-Z inhibited the rate of FX activation was 78 +/- 3 and 89 +/- 6%, resp. The degree of inhibition of the rate of FX activation correlated with a max. fold prolongation in the PT assay of 1.8-fold for A-183 and 3.3-fold for A-100-Z. The A-series peptides represent a new class of peptide exosite inhibitors that are capable of attenuating, rather than completely inhibiting, the activity of TF.cntdot.FVIIa, potentially leading to anticoagulants with an increased therapeutic window.

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS

PY 2001

2002

PATENT NO. KIND DATE

PI WO 2001010892 A2 20010215

EP 1203014 A2 20020508

IN Dennis, Mark S.

TI Factor VIIa antagonists for diagnostic or therapeutic use

SO PCT Int. Appl., 80 pp.

08/03/01

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CODEN: PIXXD2

AB This invention provides novel compds. which prevent or block a FVIIa mediated or assocd. process or event such as the catalytic conversion of FX to FXa, FVII to FVIIa or FIX to FIXa. In particular aspects, the compds. of the invention bind Factor VIIa (FVIIa), its zymogen Factor VII (FVII) and/or block the assocn. of FVII or FVIIa with a peptide compd. of the present invention. The invention also provides pharmaceutical compns. comprising the novel compds. as well as their use in diagnostic, therapeutic, and prophylactic methods.

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